SPRING 2025

INSIDE

FSIG Connection

News from the Fabry Support & Information Group

After two strokes, a diagnosis of Fabry—and chance for hope

By Jireh S.
Fabry Patient
Insta: @jireh.recaps

My Fabry journey started early one Saturday morning—Dec. 4, 2021, when I was 30 years old. We were preparing to celebrate my son's first birthday. It was the morning of what should have kicked off a weekend of celebrations.

However, at around 3 a.m., I screamed in my sleep, and it woke my wife up. I was not responding to her cry to wake me up, and thankfully, my sister-in-law was able to dial 911.

Upon EMS arrival, I was a bit more responsive answering their questions, but my speech was close to incoherent. My ER notes state that I lost consciousness again on my way to the hospital, and upon arrival, I was only responsive to pain.

The ER team was able to quickly get a CT of my head, which confirmed a subarachnoid hemorrhage—a rupture in one of the vessels that supplies blood to the part of the brain responsible for regulating breathing, consciousness, blood

Jireh with his wife and son, one month before his brain aneurysm

See HOPE, Page 2

Woman gets diagnosis only after hitting 7 symptoms

By Katherine Poinsatte, PhD
FabryDiseaseNews.com

(Oct. 18, 2024) A wide array of symptoms that affected the kidneys and cardiovascular and nervous systems led to a diagnosis of Fabry disease for a 32-year-old woman, a study in India shows.

Given that Fabry has been historically considered a male disease and that women carrying a Fabry-causing mutation may not develop the disease, the case "underscores the importance of maintaining a high index of suspicion for Fabry disease, even in female patients," wrote the researchers, who said the case also emphasizes "the need for a comprehensive diagnostic approach to ensure timely diagnosis and appropriate management."

The case study, "Fabry Disease in a Female: A Unique Case Highlighting the Variability in Clinical Presentation," was published in Cureus.

Researchers in India describe

See DIAGNOSIS, Page 3

10-year-old diagnosed with two rare conditions at once

Unusual case marks first time Fabry co-occurs with congenital form of anemia

By Andrea Lobo, PhD
FabryDiseaseNews.com

(Nov. 14, 2024) A 10-year-old boy diagnosed with Fabry disease was also found to have a rare blood disorder called congenital dyserythropoietic anemia (CDA) in a case researchers said was highly unusual.

In CDA, anemia, that is, a shortage of red blood cells that transport oxygen in the bloodstream, results in symptoms like fatigue, weakness, and pale skin.

"CDA ... and [Fabry disease] co-occurring in the same patient is a very rare medical finding [that] has never been reported," the researchers wrote. "This case ... underscores the need for further investigation into potential genetic and [disease-causing] links between these seemingly disparate conditions."

Read full story: bit.ly/Fabry-Blood

WELCOME

Dear Friends,

We're excited to keep you informed about the latest developments in Fabry disease research and treatment. Recent studies highlight the importance of early intervention, as strokes can occur at younger ages in those with Fabry disease. New potential biomarkers could mean a new tool for diagnosis and personalized treatment plans.

Maintaining treatment is crucial for managing symptoms and reducing complications, and emerging research suggests that possible changes in treatment frequency could make life easier for patients. The FDA is also open to receiving gene therapy trial data, offering hope for groundbreaking advancements in treatment options.

However, a lack of awareness and understanding often impacts the quality of life for those affected by Fabry disease. We're committed to raising awareness and providing the resources you need to stay informed.

Jack

Jack Johnson,
Executive Director

RELATED STORY

Woman receives Fabry diagnosis only after stroke at 41

A Fabry disease diagnosis for a woman in Portugal came only after she had a stroke in her early 40s, according to a new report in which the scientists highlighted "the importance of early diagnosis," especially in nontypical cases.

Read full story: bit.ly/Fabry-Stroke

HOPE: continued from p. 1

Jireh's extended family at the 2024 Fabry Walk

pressure, heart rate and sleep. Cases with my presentation and type of bleeding account for a 50-80% mortality rate.

The ER team looked to transfer me into the hospital's neuro intensive care unit for emergency surgery, but no beds were available. They found an open bed at a different hospital later that morning, and they placed a breathing tube to help stabilize me.

After multiple attempts and almost a week after my initial brain bleed, swelling in my brain decreased enough so doctors could successfully place a stent in the ruptured artery. I was in the ICU for two weeks, followed by another week in their neuro-observation unit, before I was discharged home. I was able to celebrate Christmas and my son's birthday with my family—even though a little later than we planned.

When the holidays ended, my schedule would be full of doctor visits with many different specialists—one being a geneticist. When I was in the ICU, it was recommended to see a geneticist after discharge, as the treating doctors suspected a gene mutation could have been an underlying reason for the abnormal and weakened blood vessels.

But during the medical workup, I suffered another stroke in February 2022. I remember waking up to use the bathroom, and after washing my hands, I suddenly couldn't walk. ER doctors originally sent me home, but my wife knew something was still wrong. She reached out to my neuro-interventional radiologist, who told me I should go back for an MRI. Almost 24 hours after my initial symptoms, an MRI confirmed that there was a blockage of blood flow to my brain, which led to my second stroke.

After that, my geneticist tested a second gene panel. In March 2022, the results showed that I had Fabry disease. I was relieved that they found a diagnosis and could now move toward a treatment plan.

In the months following my Fabry diagnosis, I would progress through rehab from my strokes and receive infusions. I finally felt I could see the light at the end of this tunnel.

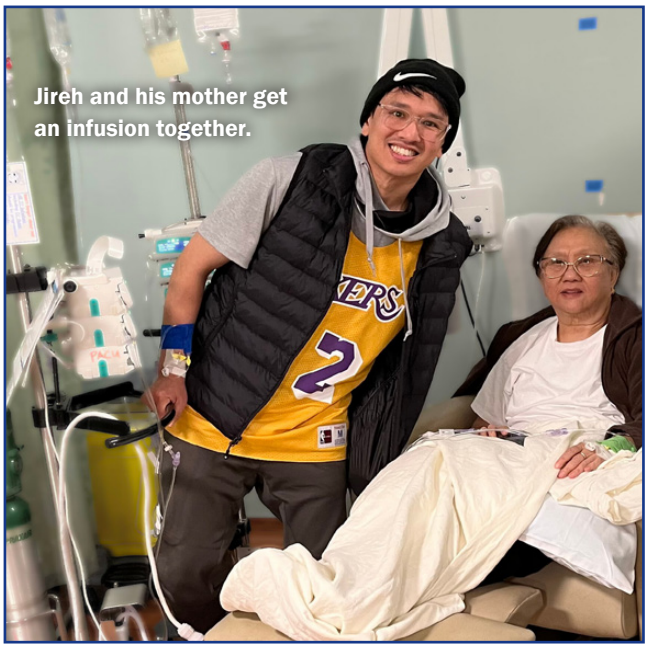
But after 6 months of medical leave from my nursing job, I was informed they could not accommodate my position. The same precautions that prevent me from carrying our son also prevented me from returning to my job.

It's now been three years since diagnosis and ongoing infusions. I've seen that through difficult circumstances comes growth and new opportunities. Since I was the first to be diagnosed, I've been able to help my mom and other family members get diagnosed and properly treated. This journey has helped me see life through a different lens—learning to focus on the things I can do and let go of the things that I cannot.

Recovery is not a linear process, and that the grief of remembering life prior to my diagnosis will always be there. However, I am thankful for the new opportunity at life—opportunity that I can still hang on to hope. That no matter how hard some days can be, I know that God has provided me with a loving family, supportive friends and a rare disease community that I can lean on.

No matter what our abilities are, we can still live each day with purpose. We can live faithfully in having a hopeful tomorrow. Having a rare disease doesn't have to define our life. It's how we choose to live each day.

"Be joyful in hope, patient in affliction, faithful in prayer" – Romans 12:12



Jireh and his mother get an infusion together.

New algorithm uses infrared patterns to spot Fabry

'Fast, inexpensive, minimally invasive technique' proven successful in both sexes

By Margarida Maia, PhD
FabryDiseaseNews.com

(Nov. 29, 2024) A machine learning algorithm to find patterns in data from infrared spectroscopy—a technique that can provide a molecular fingerprint by looking at how molecules in a sample take up light and reflect it—correctly distinguished people with Fabry disease from healthy adults in a pilot study, regardless of sex.

"It is a fast, inexpensive, and minimally invasive technique applicable to both sexes," the researchers wrote in "Infrared spectroscopy as a new approach for early Fabry disease screening: a pilot study," which was published in the *Orphanet Journal of Rare Diseases*.

Diagnosing Fabry usually involves testing the activity levels of the alpha-Gal A enzyme in a small sample of blood. However, this enzyme activity test has limitations, especially for female patients, whose levels may appear normal despite having the disease.

Researchers in Brazil used a type of infrared spectroscopy called attenuated total reflection Fourier-transform infrared (ATR-FTIR) spectroscopy to reveal disease-specific patterns in the molecules present in blood samples from 47 people with classic Fabry disease and compared with samples from 52 matched healthy individuals.

This technique works by shining infrared light onto a sample that is placed on a crystal surface. The infrared light interacts with the sample's molecules, causing them to vibrate. As the infrared light exits the crystal, it carries information about these molecular vibrations, which is then analyzed using a detector and converted into a spectrum.

Both groups had a similar percentage of females (59.6% vs. 65.4%) and a similar average age (39.2 vs. 36.7 years). Male patients had more severe symptoms than females, but even within the same family, symptoms varied widely. The kidneys were the most affected organ.

A computational algorithm capable of identifying a specific biomolecular signature for a disease with multifactorial clinical conditions has the potential to achieve greater sensitivity than a single biomarker," the researchers wrote.

Read full story: bit.ly/FabryFingerprint

Age variations hinder diagnosis

By Melissa James
FSIG Contributor

Rare diseases are difficult enough to diagnose, points out a December article from Korea Biomedical Review, but some have symptoms that change with age, making diagnosis even more difficult.

"Fabry is a disease where family testing is very important," said Professor Sohn Young-bae of the Department of Medical Genetics at Ajou University Hospital, on the Korean Organization for Rare Diseases' YouTube channel "Angels Spoon TV."

"According to reports from other countries, once a Fabry disease patient is diagnosed in a family, there are about five additional patients in the family, and there are likely other hidden patients in the family who have not been diagnosed because of the mild symptoms."

"It is often difficult to reverse Fabry disease once it has been delayed and the patient's condition has deteriorated, so it is very important to test early and start treatment early," he said."

Read full story: bit.ly/Fabry-Age

DIAGNOSIS: continued from p. 1

the rare case of a 32-year-old woman with Fabry disease who showed a wide range of symptoms.

The woman sought medical treatment at an emergency room because of progressive shortness of breath for 10 days, a fever for four days, and headache, lower limb pain, and swelling around the eye for three months. She'd previously been diagnosed with high blood pressure (hypertension) and chronic kidney disease.

An examination confirmed hypertension and fever, and showed her heart rate and breathing were abnormally fast. She also reported parasthesia, or sensations of tingling, burning, prickling, itching, or numbness. Bloodwork showed the woman had lower levels of hemoglobin, the protein in red blood cells that transports oxygen throughout the body.

Further analysis revealed substantial impairments in her kidney function, based on elevated protein levels in the urine and elevated levels of urea and creatine in the blood.

A kidney biopsy was taken to identify the underlying cause of these issues and clinicians found increased tissue stiffness in her kidneys and larger than normal podocytes, a type of kidney cell that wraps around blood vessels to help filter waste and fluid from the blood. Kidney cells also showed zebra bodies, a hallmark of Gb3 buildup in cells.

The findings, along with her symptoms, led clinicians to diagnose the woman with Fabry disease.

Read full story: bit.ly/FabryFemale

Long-term ERT normalizes inflammation

Study finds treatment over time produces sustained benefits

By Steve Bryson, PhD
FabryDiseaseNews.com

(Nov. 21, 2024) Long-term enzyme replacement therapy (ERT) normalizes markers of inflammation and oxidative stress in adults with Fabry disease, a study found.

"These findings lead us to believe that long-term ERT can improve the redox status and protect these individuals against oxidative ... stress, as well as the inflammatory process," researchers wrote in the study, "Long-term enzyme replacement therapy in Fabry patients protects against oxidative and inflammatory process," which was published in *Naunyn-Schmiedeberg's Archives of Pharmacology*.

In ERT, the standard Fabry treatment, a lab-made version of the alpha-Gal A enzyme is infused directly into the bloodstream. This helps the body break down Gb3, easing symptoms and delaying potentially life-threatening disease complications. Fabrazyme (agalsidase beta) and Elfabrio (pegunigalsidase alfa-iwxj) are two ERTs currently approved in the U.S.

Because Gb3 deposition also promotes a pro-inflammatory state in some patients, scientists in Brazil assessed the effects of ERT on inflammation and oxidative stress, a type of cell damage that occurs when reactive oxygen species outweigh the body's antioxidant defenses.

No differences were noted between men and women patients and controls regarding the activity of the NF-kappaB gene, which encodes a protein that participates in a pro-inflammatory signaling pathway in white blood cells.

Likewise, the levels of two oxidative stress markers, thiobarbituric acid-reactive species (fat oxidation) and urinary nitrite, were similar across all groups. A third marker for protein oxidation was lower in men with Fabry than controls.

"Our results suggest that long-term ERT in men with [Fabry] contributes to the reduction of a pro-inflammatory scenario and a decrease of oxidative damage in patients, reflecting greater control throughout the disease and in the multisystemic changes characteristic of this disorder," the authors wrote.

Read full story:
bit.ly/LTERT

Less frequent Elfabrio appears safe, effective

By Margarida Maia, PhD
FabryDiseaseNews.com

(Nov. 1, 2024) Treatment with Elfabrio (pegunigalsidase alfa), given at more spaced intervals and at a higher dose than that approved for Fabry disease, appears to be safe and effective for adults with stable disease, data from a Phase 3 clinical study suggests.

Developed jointly by Chiesi Global Rare Diseases and Protalix Biotherapeutics, Elfabrio is approved in the U.S., the European Union, and the U.K for infusion into a vein at a recommended dose of 1 mg/kg every other week. The goal of the BRIGHT (NCT03180840) study was to test if Elfabrio could be taken at less frequent intervals.

The study included a small number of patients, so more research is needed, but "Chiesi is committed to evaluating additional evidence to confirm the long-term results of this administration schedule," Giacomo Chiesi, executive vice president of Chiesi Global Rare Diseases, said in a company press release.

The results of the study, "A phase III, open-label clinical trial evaluating pegunigalsidase alfa administered every 4 weeks in adults with Fabry disease previously treated with other enzyme replacement therapies," were published in the Journal of Inherited *Metabolic Disease.European Medicines Agency.*

The European Medicines Agency (EMA) has validated a regulatory application that seeks clearance of this less frequent regimen of Elfabrio.

If the agency decides to approve the variation application after its review, Fabry patients in the European Union could start receiving the therapy once every four weeks, at a dose of 2 mg/kg.

"The validation of this variation application is an important milestone in our efforts to reduce the burden of treatment for some adult patients living with Fabry disease who continue to experience unmet medical needs," Giacomo Chiesi, executive vice president of Chiesi Global Rare Diseases, which codeveloped the therapy with Protalix Biotherapeutics, said in a joint company press release.

Read full stories:
bit.ly/ElfabrioDosing
bit.ly/ElfabrioERT

German study: ERT advice stabilizes Fabry in women

Participants enjoy a game last November at the Fabry Women's Summit in San Antonio, Texas.

Steve Bryson, PhD
FabryDiseaseNews.com

(Jan. 23, 2025) Women severely affected by Fabry disease and treated with enzyme replacement therapy (ERT) and untreated women with less severe symptoms showed broadly stable disease course over five years, a study in Germany found.

Treatment decisions were primarily based on the European guidelines for females with Fabry, which recommend initiating treatment at the first manifestation of Fabry-related organ involvement or pain. The guidelines "appear to have been correct" for most of the women in the study, the researchers wrote. Still, "it is crucial to explore if organ involvement is [Fabry]-related in order to make the correct treatment decision," they wrote.

The study, "Impact of enzyme replacement therapy on clinical manifestations in females with Fabry disease," which was published in the *Orphanet Journal of Rare Diseases*.

According to current European guidelines, ERT for female Fabry patients should start after the first manifestation involving the kidneys, heart, or nervous system, or if pain or severe gastrointestinal complaints are present.

Because the GLA gene is located on the X chromosome, males with one copy of the gene tend to have more severe symptoms that develop earlier than females with two copies. For females, even if one copy of the GLA gene is mutated, the second copy is typically normal, so disease onset, progression, and severity varies more than in males.

A previous study suggested that treatment for women with Fabry generally aligns with current European guidelines—yet one-third of patients were left untreated despite organ involvement.

The researchers said this discrepancy means more data are required for female patients to analyze the effect of ERT or to exclude potential disease progression in untreated females. They retrospectively analyzed data from 159 women with Fabry collected at three visits at six Fabry centers in Germany. All participants were either untreated with ERT or on a stable dose of agalsidase alfa, sold as Replagal outside the US or agalsidase-beta, sold as Fabrazyme, for at least six months.

Seventy-one patients were untreated, 47 were newly treated, and 41 had received long-term ERT. The untreated group was significantly younger, had the lowest blood levels of lyso-Gb3, and had the least frequent Fabry-related symptoms and manifestations, including edema (swelling), pain, fatigue, and heart involvement.

The newly ERT-treated group had the highest blood pressure values and showed more frequent albuminuria, a sign of kidney disease. Median eGFR values, a test for kidney function, and the number of ischemic attacks/strokes were similar before the first visit across all three groups.

Fabry-related pain was the most frequent initial manifestation in all three groups, followed by heart and kidney involvement.

Read full story:
bit.ly/FabryStable

Teva's Galafold generic may be available in US

Clearance expected by 2037 if FDA OKs

By Marisa Wexler, MS
FabryDiseaseNews.com

(Nov. 7, 2024) Amicus Therapeutics and Teva Pharmaceuticals have struck a deal that will allow the latter to sell a generic version of Galafold (migalastat), Amicus' chaperone therapy for Fabry disease, to patients in the U.S.

Under the agreement, Teva will have its clearance on Jan. 30, 2037, assuming the U.S. Food and Drug Administration (FDA) approves the company's generic therapy and that no other issues arise in the meantime.

The generic version should have the same active ingredient, strength, route of delivery, safety, efficacy, and intended use as its brand-name alternative. Generic medicines usually come at a significantly lower cost, however.

The settlement "is a major step forward in ensuring Amicus can continue to support the Fabry community with Galafold for many years to come," Bradley Campbell, president and CEO of Amicus, said in a company financial update.

Amicus and Teva have been engaged in a legal dispute since 2020 when Teva accused Amicus of refusing to provide access to enough Galafold samples for studies that could determine the equivalence of Teva's generic formulation.

While the dispute ended the following year, Teva submitted an application to the FDA in 2022 seeking approval of its Galafold generic before Amicus' patents on the medication had expired.

Read full story:
bit.ly/Galafold2037

Fabry gene therapy study data sufficient for FDA submission

Findings could accelerate ST-920 approval

By Margarida Maia, PhD
FabryDiseaseNews.com

(Oct. 25, 2024) Data from an ongoing Phase 1/2 clinical study of ST-920 (isaralgagene civaparvovec), an investigational gene therapy for Fabry disease, could serve as the main evidence for its accelerated approval by the U.S. Food and Drug Administration (FDA), eliminating the need for an additional registrational study to confirm its clinical benefit.

The full dataset from STAAR (NCT04046224), which is needed for the accelerated approval, will be ready in the first half of 2025, enabling developer Sangamo Therapeutics to seek a biologics license application by the second half of the year, three years earlier than expected. This could shorten the time for ST-920 to enter the market.

In an earlier meeting, the FDA agreed a well-controlled registrational study, along with existing data, could be sufficient as the basis for ST-920's approval, but it's now providing an alternative clear regulatory pathway to accelerated approval, which grants a go-ahead based on a surrogate marker that's thought to predict clinical benefit.

"I strongly believe in the potential for ST-920 to alleviate many manifestations of Fabry disease and am delighted to have a clear regulatory pathway that could bring this treatment to patients significantly sooner than originally anticipated," Sandy Macrae, PhD, Sangamo's CEO, said in a company press release.

Fabry disease is caused by mutations in the GLA gene, which provides instructions for producing alpha-Gal A, an enzyme that works to break down fatty molecules. When the enzyme is faulty, the molecules build up to toxic levels in cells, leading to progressive organ damage, particularly affecting the heart, kidneys, and nervous system, and resulting in a range of symptoms.

Infused as a single dose into the bloodstream, ST-920 is designed to deliver a healthy version of GLA to liver cells so they can produce a working alpha-Gal A enzyme on their own to support the breakdown of fatty molecules like Gb3 and help alleviate symptoms. STAAR is testing the safety and tolerability of ST-920 in 33 men and women with a diagnosis of Fabry disease. The patients are being followed for 52 weeks, after which they can enter a five-year extension. The patient who's been in the study the longest recently completed four years of follow-up.

Interim data showed ST-920 was well tolerated, with the most common side effects being fever, headache, viral infection, fatigue, and cold-like symptoms. All the participants showed a sustained increase in alpha-Gal A enzyme levels and saw their symptoms become less severe.

All 18 patients who started the study on ERT were able to stop it. The patients' alpha-Gal A levels remained at normal or above-normal despite being off ERT.

Nearly all Fabry patients have kidney problems, such as passing protein into the urine or a reduced glomerular filtration rate (eGFR), an indicator that the kidneys aren't filtering blood as well as they should, that sometimes leads to kidney failure. The 18 patients with a year+ of follow-up had significant improvements in eGFR, suggesting better kidney function.

Read full story: bit.ly/FabryData

BRIEFS

New gene therapy EXG110 gains FDA orphan drug status

(Dec. 5, 2024) The U.S. Food and Drug Administration has granted orphan drug designation to EXG110, an experimental gene therapy for Fabry that's being developed by Exegenesis Bio and is currently in clinical testing.

The FDA's orphan drug status gives economic incentives to companies that are investing in the development of new treatments for rare diseases—which by definition have a small market size that can make it difficult to recoup investment and turn a profit.. Treatments given this designation are guaranteed seven years of market exclusivity if they are ultimately approved by the FDA.

"The FDA's decision to grant orphan drug designation to EXG110 highlights the need for better approaches to treat Fabry disease," said Zhenhua Wu, PhD, Exegenesis' CEO, in a press release.

Read full story: bit.ly/EXG-110

4DMT freezes gene therapy funds for 4D-310

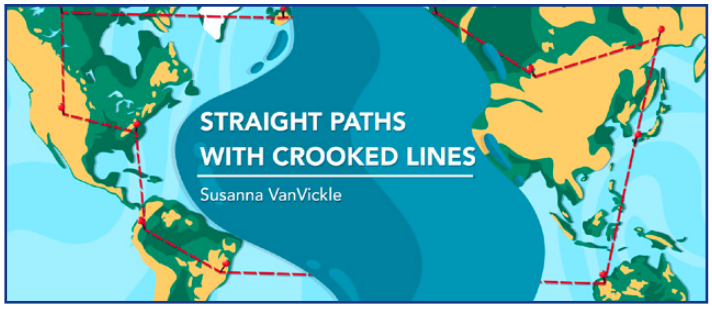
(Dec. 5, 2024) 4D Molecular Therapeutics is nixing two clinical programs and cutting off funds for three other assets to focus on the biotech's eye disease gene therapy, 4D-150.

The programs with halted funding—pending additional financing or partnerships—include an ongoing phase 1/2 trial assessing 4D-310 for Fabry disease-related cardiomyopathy.

The genetic medicines biotech has also decided not to invest anything into new preclinical candidates for the time being. The company said it's currently exploring partnership prospects and other financing options.

Read full story: bit.ly/4DMT2028

Fabry can't dampen my kids' adventurous spirit



By Susanna VanVickle
FabryDiseaseNews.com

(Oct. 29, 2024) I grew up in a missionary family, and we were constantly moving. By the time I was in the fourth grade, we'd lived in six different countries. Moving around the world, experiencing new cultures, and interacting with all kinds of people were formative for me.

My own children haven't had the international upbringing that I did, but I do want them to experience the world. In fact, when my twin sons, Michael and Anthony, were diagnosed with Fabry and told they'd need to be treated with enzyme replacement therapy for life, one of the first questions we asked was how it'd affect their ability to travel. I wanted them to inherit more than a gene mutation from me; I'd hoped they'd also acquire my adventurous spirit.

In 2023, both Michael and Anthony were able to travel abroad for a semester: Anthony studied at Benedictine College's campus in Florence, Italy, and Michael studied at the Franciscan University of Steubenville's campus in Gaming, Austria.

Before their first trip across the pond, the boys had to weigh the pros and cons of changing or pausing their treatment plans. Thankfully, Fabry didn't prevent them from experiencing what both of them described as their most exciting semester of college. They made wise use of the fact that they weren't being treated with ERT, which allowed them to transition into a clinical trial for an investigational Fabry treatment when they returned home.

Read full story: bit.ly/FabrySpirit

Study: Others' ignorance of Fabry impacts life quality

By Lindsey Shapiro, PhD
FabryDiseaseNews.com

(Dec. 19, 2024) In interviews, people living with Fabry disease in Spain reported a number of unmet needs—among them a general dearth of understanding of the condition's challenges—that negatively impact patient quality of life.

Topping the patients' main concerns were the scant knowledge about Fabry among work colleagues, friends, family, and others in the general population, and little empathy for those living with the disease, according to a study detailing the interview findings.

Delayed diagnoses and a lack of knowledge from medical professionals were also cited as significant concerns.

"The results of this study draw attention to the need to gain more knowledge of this disease as well as to provide support resources based on the needs of these patients ... which will help improve their quality of life and promote disease management and treatment," the researchers wrote.

Their study, "Quality of life and unmet needs in patients with Fabry disease: a qualitative study," was published in the *Orphanet Journal of Rare Diseases*."

The researchers conducted phone interviews with nine adults with the condition and one Fabry patient association representative. Following the interviews, three patients and one relative participated in a focus group to further explore the issue.

The interviewees reported a significant emotional impact of Fabry on themselves and their loved ones. As such, they said they often had feelings of anxiety, depression, anger, and/or frustration, as well as fear or concern about how the disease would evolve.

"I have very severe depression ... I don't have a 100% normal life like other people ... my mood is not like other people's ... it is a state of apathy, of sadness ... of not being at ease and of feeling empty ... of not being able to do everyday things," one interviewee said.

The patients reported a wide range of adjustments that needed to be made after a Fabry diagnosis, in terms of daily and social activities, work life, and family roles or expectations.

They also showed significant concern when thinking about having children or having existing children tested for Fabry, given the disease's genetic nature.

To deal with these emotional emotional impacts, patients reported using a variety of different management strategies. Patient associations, in particular, were a valuable resource, offering an opportunity to share experiences with others who understand the Fabry journey.

Read full story: bit.ly/FabryQoL

FSIG

FSIG is a support group dedicated to dispensing information and encouraging mutual self-help as a means of emotional support.

FSIG was formed in 1996 by two Fabry patients and supportive family members with the hope that their particular understanding of this disease, combined with experience gathering information and working with doctors could benefit others.

FSIG is a nonprofit, tax-exempt organization and relies on charitable contributions to provide services to those with Fabry disease, their families and supportive others. Donations may be sent to the address below.

Please feel free to make copies of the FSIG Newsletter to share with your family, friends and others. We encourage anyone interested in FSIG or the newsletter to contact us so we can make sure you receive the next issue.

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Glafabra secures rights to novel vector for treating enzyme deficiency diseases

Biotech will collaborate with university on trials

PRESS RELEASES

(Jan. 6 & 11, 2025) Glafabra Therapeutics has secured exclusive rights to a cutting-edge technology that enables the creation of a "lentivector-transgene combination."

According to Dr. Chris Hopkins, the CEO of Glafabra, "Access to this innovative vector backbone will allow the creation of more effective LV gene therapies and allow Glafabra to better address the unmet needs in enzyme deficiency diseases." This breakthrough development opens up new possibilities for the treatment of various genetic diseases, providing hope for patients in need of advanced medical solutions.

Patients who have undergone treatment with Glafabra's LV gene therapy for Fabry disease have reported remarkable improvements in their health and quality of life. One patient expressed their gratitude by stating, "The stem cell transplant with LV gene therapy has made me literally feel like I have no disease, and my life became so much more normalized than before."

Building on its success in Canadian clinical studies, Glafabra is now exploring opportunities to establish clinical sites in the USA. The company aims to introduce their clinically-demonstrated therapy for Fabry disease to American patients and ease their therapeutic burden with a one time transfusion that last for at least 5 years.

In related news, Glafabra has entered into a letter of intent with the University of Utah—specifically through its Utah Data Coordinating Center (Utah DCC) and Cell Therapy and Regenerative Medicine Program (CellReGen™)—to collaborate on accelerating the development of this potential new treatment.

Read full story: bit.ly/Glafabra

Drug makers share clinical trial progress

Lucerastat Phase 3 results presented at ASN Kidney Week

(Oct. 16, 2024) Data from the Phase 3 program with Idorsia's lucerastat will be presented as a poster at the American Society of Nephrology (ASN) Kidney Week 2024. The event will be held in San Diego, CA, Oct. 23–27.

Lucerastat is Idorsia's oral inhibitor of glucosylceramide synthase, offering a potential new treatment approach for all patients living with Fabry disease, irrespective of the mutation type of the GLA gene.

Analysis of the ongoing open-label extension (OLE) of the Phase 3 study corroborated the longterm effect on plasma Gb3 levels and a potential positive long-term effect on kidney function. The analysis also showed a safety and tolerability profile consistent with that observed during the 6-month randomized treatment period.

Read full story: bit.ly/luceraP3

Chiesi publishes Phase 3 trial results for Elfabrio®

(Oct. 28, 2024) Chiesi Global Rare Diseases announced today the publication of results from the Phase 3 BRIGHT study of Elfabrio—2 mg/kg administered every four weeks for 52 weeks in adult patients with Fabry disease who were previously treated with agalsidase alfa or beta, administered every two weeks.

The approved dose of Elfabrio is 1mg/kg every two weeks. The regimen of Elfabrio 2mg/kg administered every four weeks is investigational and not approved by the FDA.

The results show that 2 mg/kg administered every four weeks is generally well-tolerated in stable adult ERT-experienced patients with Fabry, a schedule the company said deserves further exploration through additional research.

Read full story: bit.ly/P3Bright

Global trials begin for subcutaneous monthly treatment

(Jan. 13, 2025) Hanmi Pharm and GC Biopharma are entering global phase 1/2 global clinical trials for LA-GLA, a once-monthly subcutaneous treatment for Fabry disease.

The trial, approved by the South Korea last Thursday and by the U.S. FDA in August 2024, will evaluate the treatment's safety, tolerability and efficacy.

LA-GLA is designed as a next-generation extended enzyme replacement therapy, offering improved durability, safety, and convenience, reports the company. LA-GLA received Orphan Drug Designation from the FDA in May 2024.

Hanmi Pharm plans to present three preclinical studies at the WORLDSymposium 2025, highlighting improved outcomes in kidney function, vascular health and peripheral nerve disorders.

Read full story: bit.ly/Hanmi-GC

LEGAL UPDATES

Amicus settles patent suit over Teva's generic Galafold

(Oct. 17, 2024) On Thursday, Amicus Therapeutics announced it has signed a license agreement with Teva Pharmaceuticals.

This new agreement resolves the patent lawsuit Amicus filed in response to Teva's Abbreviated New Drug Application to market a generic version of Galafold (migalastat) 123mg capsules before the expiration of the applicable patents.

Amicus will permit Teva a license to market its generic version of Galafold in the U.S. starting Jan. 30, 2037, pending FDA approval (and unless certain circumstances customarily included in these types of agreements take place).

Industry leaders are reminding the public that the FDA's approval of Teva's generic version of Galafold is not guaranteed and is subject to the regulatory body's standard review process. The specific financial details of the agreement have not been disclosed.

Read full story: yhoo.it/4hQDmoZ

AMT-191 maker uniQure commences public offering

(Jan. 7, 2025) uniQure N.V., a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced that it has commenced an underwritten public offering of its ordinary shares and pre-funded warrants to purchase its ordinary shares.

All securities to be sold in the offering will be offered by uniQure.

In addition, uniQure intends to grant the underwriters a 30-day option to purchase up to 15% additional ordinary shares at the public offering price, lessunderwriting discounts and commissions. The offering is subject to market and other conditions, and there can be no assurance as to whether or when the offering may be completed, or as to the actual size or terms of the offering.

Patient enrollment in the clinical trial of AMT-191, uniQure's gene therapy candidate for the treatment of Fabry disease, began in 2024. AMT-191 is an investigational AAV5 gene therapy that delivers a GLA transgene designed to target the liver to produce GLA protein.

In patients with Fabry disease, a pathogenic variant in the GLA gene leads to GLA enzyme deficiency which results in a progressive accumulation of lipids in multiple cell types creating a multi-system disorder. AMT-191 represents a novel potential one-time administered approach to treating Fabry disease.

Read full story: bit.ly/uniquirepo

Pathway cleared for ST-920 FDA Accelerated Approval

(Oct. 22, 2024) Sangamo Therapeutics, Inc., today announced the outcome of a recent successful interaction with the U.S. FDA, providing a clear regulatory pathway to Accelerated Approval for isaralgagene civaparvovec, or ST-920, its wholly owned gene therapy product candidate for the treatment of Fabry disease.

The FDA has agreed in a Type B interaction that data from the ongoing Phase 1/2 STAAR study can serve as the primary basis for approval under the Accelerated Approval Program, using eGFR slope at 52 weeks across all patients as an intermediate clinical endpoint. The complete dataset to support an Accelerated Approval pathway will be available in the first half of 2025. This approach unlocks a potential BLA submission in the second half of 2025, three years ahead of previous estimates, and avoids the requirement for an additional registrational study to establish clinical efficacy.

Sangamo engaged with the FDA on alternative pathways to potential approval following analysis of clinical data from the Phase 1/2 STAAR study showing encouraging safety and efficacy data, including promising preliminary evidence of improved kidney function. Renal manifestations, such as asproteinuria or a decreased glomerular filtration rate, occur early in life in almost all male, and in many female, patients with Fabry disease, and can lead to end-stage renal disease and early death. In the 18 male and female patients treated with isaralgagene civaparvovec with more than one year of follow-up data, statistically significant improvements were observed in both mean and median eGFR levels, resulting in a positive annualized eGFR slope.

Based on these latest data, the FDA agreed that eGFR slope at 52 weeks can serve as an intermediate clinical endpoint to support a potential Accelerated Approval. The FDA also advised that eGFR slope at 104 weeks may be assessed to verify clinical benefit.

Read full story: bwnews.pr/4bOY6vx

FABRY IN THE NEWS

Students from the Medical University of Vienna who won second place at the Jakob Henle Contest in Germany, which featured rare disease diagnoses.

MY SCIENCE

Students diagnose Fabry in medical skills competition

(Nov. 22, 2024) A team from the Medical Unversity of Vienna took second place in the Jacob Henle Contest in Göttingen, Germany. The Jakob Henle Contest is a competition for medical students based on the Paul Ehrlich Contest, which has been held since 1998 (originally under the name Benjamin Franklin Contest).

The participants put their skills to the test in the areas of visual diagnosis, clinical case processing, practical tasks and a complex final case. The aim is to promote medical knowledge, teamwork and practical skills in a competitive but collegial environment.

First, 12 visual diagnoses had to be solved in four rounds, in which rare or typical clinical pictures had to be recognized at lightning speed using images. Three clinical cases had to be correctly diagnosed. For example, there were patients with Graves' disease. In addition, two written cases had to be solved in which the teams had to create a suspected diagnosis, differential diagnoses, further diagnostics and a treatment plan from given findings. Knowledge of aortic stenosis and Fabry disease was required.

Read full story: bit.ly/myscifabry

PHYSICIANS WEEKLY

The pathogenic role of misprocessed α-GAL A

(Nov. 21, 2024) Researchers conducted a retrospective study on Fabry disease and found endoplasmic reticulum stress contributing to its pathogenesis.

They analyzed 30 individuals, including 6 with kidney failure and 24 family members, using genetic, clinical, biochemical, and molecular methods to characterize the p.L394P alpha-galactosidase A variant.

They found defective proteostasis of mutated alpha-galactosidase A causing chronic endoplasmic reticulum stress and unfolded protein response. They concluded this as a key contributor to Fabry disease pathogenesis.

Read full story: bit.ly/AGA-Role

LOVELL CHRONICLE

Fabry expert joins cardiology staff at Wyoming hospital

(Jan. 3, 2025) After 14 years of serving patients as a visiting specialist through Billings Clinic (Montana), cardiologist Dr. Kristin Scott-Tillery has officially joined the staff at North Big Horn Hospital in Lovell, Wyoming.

Scott-Tillery specializes in treatment of heart failure, transplant cardiology and cardiovascular disease. She is a nationally known expert in Fabry disease, a rare genetic disorder that causes valves in the heart to retain waste products, leading to medical complications. She speaks nationally on the subject.

She said she originally wanted to specialize in neurology but chose to specialize in cardiology instead because she felt it was an area of medicine where she could do more to help people.

Read full story: bit.ly/NBHH-Cardio

GREENVILLE NEWS

Spotlight features physician with Fabry, Testing for Tots

(Dec. 20, 2024) Brian Jones knows when it's time for his treatment, reported the Greenville (South Carolina) News.

Fatigue and pain remind him even if the calendar does not. But Brian, an Asheville, NC, physician specializing in nephrology, is grateful that his lifelong health issues have a name—and a path forward.

He and his wife, Tia, are working hard to offer the same hope to others with his rare condition, as they advocate for newborn testing to spare the next generation from its effects.

Brian has Fabry disease, a lysosomal storage disorder that can cause a variety of symptoms.

"It's a condition where your cells are not able to break down a certain substance, and that substance just continues to build up and build up and build up until, essentially, the cell is full of that substance and it's not able to do its normal activity," he told the newspaper. "People have different analogies. When I give talks, I say it's like the trash trucks aren't working, so the trash just builds up in the streets, and then the city's not functional. "

Brian and Tia co-founded Testing for Tots, a nonprofit aimed at improving early diagnosis initiatives for Fabry disease, in 2018. A big focus of their work is having the condition added to newborn screenings, which already test for a variety of genetic conditions.

Testing for Tots offers information and support, as well as advocacy. Learn more at fabry.org/testing-for-tots.

Read full story: bit.ly/FabryOutcome

PHILIPPINE STAR

PhilHealth to offer packages with rare disease benefits

(Dec. 2, 2024) Members of the Philippine Health Insurance Corp. (PhilHealth) will soon enjoy enhanced benefit packages, which include coverage for rare diseases, expected to be available in early 2025.

The PhilHealth board has approved the new enhanced benefit packages for heart attacks, kidney disease, mobility limitations, oral health, and 10 rare diseases. Among the diseases included are Gauche, Pompe and Fabry.

Read full story: bit.ly/RareDisCov

ACKNOWLEDGEMENTS

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FSIG would like to express our gratitude to the many physicians, health care professionals, researchers, scientists, and industry working on our behalf. Their efforts make a great difference for us all.

Fabry community support & resources

Courtesy of FabryDiseaseNews.com
Fabry disease support groups can be a vital source of encouragement, guidance, and community for people living with the condition.

National Fabry support groups:
- FSIG
- National Fabry Disease Foundation (NFDF)
- Fabry Connect

International Fabry support groups:
- Fabry International Network
- Canadian Fabry Association

Those living with Fabry may also find support through organizations such as:
- American Kidney Fund
- Genetic Alliance
- National Organization for Rare Disorders
- National Kidney Foundation
- National Society of Genetic Counselors

Online support:
- Fabry Disease News
- Fabry Disease Info and Support on Facebook
- NFDF on X
- FSIG on X

Financial support:
- The Assistance Fund
- Co-Pay Relief
- PAN Foundation
- National Organization for Rare Disorders
- Fabry Assist
- Accessia Health

Find full lists & links: bit.ly/FabryGroups

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- New algorithm uses infrared patterns to spot Fabry